

Editorial

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Introduction of Chinese expert consensus on neoadjuvant therapy for primary liver cancer (2023 edition)

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BACKGROUND

Primary liver cancer is the sixth most prevalent tumor and the third leading cause of cancer-related mortality worldwide^[1]. In 2020, there were approximately 900,000 new cases of primary liver cancer and 830,000 associated deaths globally, with China accounting for nearly half of these cases. Hepatocellular carcinoma (HCC) is the most common pathological type of primary liver cancer, accounting for about 90% of primary liver cancer cases in China. Over recent years, the five-year overall survival rate following hepatectomy for resectable liver cancer has surpassed 60.0%. However, postoperative recurrence remains a significant concern, particularly among patients classified as stage IIb and IIIa according to the China Liver Cancer staging system (CNLC) in China. The one-year recurrence rates for these patients exceed 55%, while those with stage Ib and IIa experience recurrence rates of 32.4% and 45.7%, respectively^[2].

The main objective of neoadjuvant therapy is to reduce the risk of postoperative recurrence and prolong survival time in patients with primary liver cancer. However, currently, no relevant expert consensus or



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guideline is provided in related fields. Neoadjuvant therapy for primary liver cancer encompasses systemic treatment and/or local measures administered to individuals initially diagnosed with resectable high-risk recurrent factors before surgery with an expectation of achieving R0 resection, sufficient remnant liver volume, Child-Pugh grade A or part B. Its purpose is to reduce the probability of recurrence and improve overall survival^[3].

CHINESE EXPERT CONSENSUS ON NEOADJUVANT THERAPY FOR PRIMARY LIVER CANCER (2023 EDITION)

In March 2023, under the organization of Committee of Digestive Surgery of Chinese Research Hospital Association and Committee of Liver Cancer of Chinese Anti-Cancer Association, Alliance of Chinese Expert Consensus on Neoadjuvant Therapy for Hepatocellular Carcinoma was discussed and revised several times, and finally, the 2023 edition was formulated^[3]. The grading of evidence-based medicine evidence in this consensus was based on the grading of recommendations, assessment, development and evaluation (GRADE) grading and Oxford Center for Evidence-Based Medicine Grading (2011 edition), and the strength of expert recommendation was mainly based on the GRADE guiding principles for grading recommendations, in combination with the grading scheme of American Society of Clinical Oncology (ASCO) guidelines. This consensus aims to provide specific suggestions for preoperative treatment of HCC and further promote the standardization of neoadjuvant therapy of HCC.

THE INDICATION AND DURATION OF PATIENTS FOR NEOADJUVANT THERAPY

The target population eligible for neoadjuvant therapy includes: (1) Resectable CNLC Ib~IIa patients presenting risk factors such as incomplete tumor capsule formation, tumors adjacent to vessels, or alpha-fetoprotein (AFP) levels exceeding > 400 µg/L; (2) For resectable CNLC IIB~IIIa patients, participation in neoadjuvant clinical trials or undergoing neoadjuvant therapy should be considered after consultation by a multidisciplinary team (MDT).

The neoadjuvant therapy cycle for primary liver cancer is typically 6-12 weeks, with a maximum duration of 16 weeks. Regardless of whether the lesion is shrinking or not, surgery should be promptly performed once the goal of treatment has been achieved. Tyrosine kinase inhibitors (TKI) should be discontinued one week prior to surgery, while Immune checkpoint inhibitors (ICI) should be stopped four weeks before surgery. It is recommended to wait at least four weeks between surgery and the last Transarterial chemoembolization (TACE) or radiotherapy treatment. The involvement of an MDT team is essential in neoadjuvant therapy for primary liver cancer patients. The discussion should be led by hepatobiliary surgeons and include physicians from oncology, interventional therapy, radiology, radiotherapy, liver disease, gastroenterology, and pathology departments. A comprehensive evaluation must be conducted to determine if patients can benefit from neoadjuvant therapy and choose the appropriate plan based on individualized principles.

NEOADJUVANT THERAPY FOR PRIMARY LIVER CANCER AND EFFECTIVENESS EVALUATION

Simple TACE therapy is not recommended as a neoadjuvant treatment for primary liver cancer; instead, it is suggested that TACE combined with targeted and/or immune therapy serves as an alternative option. Some clinical trials have demonstrated that Hepatic arterial chemoperfusion (HAIC) as a neoadjuvant therapy for primary liver cancer can reduce postoperative recurrence rates and improve patient overall survival. Neoadjuvant precision radiotherapy, such as Stereotactic body radiation therapy (SBRT), can decrease postoperative recurrence rates in patients with portal vein tumor thrombus while improving overall survival rates. Similarly, neoadjuvant intensity-modulated radiotherapy can enhance outcomes in

central primary liver cancer cases. Neoadjuvant immunotherapy has shown potential in improving prognosis and increasing the complete pathological response(CPR) rate among patients with primary liver cancer.

The primary efficacy index of neoadjuvant therapy for liver cancer is recurrence-free survival (RFS) or progression-free survival (PFS), while secondary efficacy indexes include major pathological response (MPR), overall response rate (ORR), and time to progression (TTP). The MPR of neoadjuvant therapy for liver cancer is suggested to be defined as the proportion of residual active tumor cells $\leq 30\%$.

IMMUNE-RELATED TOXICITY AND SIDE EFFECTS (IRAES) OF NEOADJUVANT IMMUNOTHERAPY

Adverse reactions commonly observed in neoadjuvant immunotherapy for liver cancer include skin toxicity, pneumonia, endocrine system toxicity, and digestive tract toxicity. Prior to treatment initiation, it is necessary to conduct routine screening of baseline organ function through blood tests, liver and kidney and thyroid function tests, myocardial enzyme analysis, electrocardiograms, chest CT scans, and other examinations. Grade 1 irAEs typically do not require any treatment, grade 2 irAEs necessitate suspension of drug use until adverse reactions are relieved, while grade 3-4 irAEs should be treated with steroid hormones and stopped immunotherapy.

For patients who respond well to neoadjuvant therapy for primary liver cancer, it is recommended to continue with the original plan as postoperative adjuvant therapy after surgery. The selection of treatment plans should balance and consider both effectiveness and safety. In cases where neoadjuvant therapy fails, individualized follow-up treatment strategies should be chosen based on previous treatments and disease progression with MDT. Local therapies or radiotherapy, along with targeted therapy and immunotherapy, have shown promising results in the field of neoadjuvant therapy for primary liver cancer. The efficacy, safety profile, and unique advantages associated with neoadjuvant therapy suggest its potential as a future development direction in the treatment of primary liver cancer. However, more high-quality clinical trials are needed to provide solid evidence-based support for neoadjuvant therapy in reducing post-surgical recurrence rates and improving long-term survival rates among patients with primary liver cancer.

DECLARATION

Authors' contributions

Lead the introduction of the consensus framework, organize text on consensus introduction, and review the final version: Liu L

Review the literature, write the first draft of introduction of the consensus, and finalization: Wang J

Availability of data and materials

Not applicable.

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Conflicts of interest

Both authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71:209-49. [DOI](#)
2. Liu Y, Liu L. Changes in the epidemiology of hepatocellular carcinoma in Asia. *Cancers* 2022;14:4473. [DOI](#)
3. Alliance of Chinese Expert Consensus on Neoadjuvant Therapy for Hepatocellular Carcinoma, Committee of Digestive Surgery of Chinese Research Hospital Association, Committee of Liver Cancer, Chinese Anti-Cancer Association. [Chinese expert consensus on neoadjuvant therapy for hepatocellular carcinoma (2023 edition)]. *Zhonghua Wai Ke Za Zhi* 2023;61:1035-45. [DOI](#)